An early T cell lineage commitment checkpoint dependent on the transcription factor Bcl11b.

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Public Summary:
Although many factors are known to be necessary for development of the immune cells called T cells, there have remained a number of mysteries about how these factors actually work. It is known that blood-cell precursors begin to develop into T cells but for some time preserve the ability to change paths and develop into some other cell types instead. The decision to develop as a T cell is only finalized during a specific commitment process. Until now, it has been unknown what protein factors cause blood-cell precursors to become committed to develop into T cells. This paper identifies the regulatory factor called Bcl11b, a gene expression control protein, as a crucial and unique factor that is needed to make T-cell commitment possible. This factor is turned on for the first time in the precursors when they are ready to become committed and then remains on through the life of the T cells. This paper shows that Bcl11b is the critical factor that is needed to enable the cells to turn off stem-cell genes, give up immature-cell growth properties, and give up the ability to change developmental path.

Scientific Abstract:
The identities of the regulators that mediate commitment of hematopoietic precursors to the T lymphocyte lineage have been unknown. The last stage of T lineage commitment in vivo involves mechanisms to suppress natural killer cell potential, to suppress myeloid and dendritic cell potential, and to silence the stem cell or progenitor cell regulatory functions that initially provide T cell receptor-independent self-renewal capability. The zinc finger transcription factor Bcl11b is T cell-specific in expression among hematopoietic cell types and is first expressed in precursors immediately before T lineage commitment. We found that Bcl11b is necessary for T lineage commitment in mice and is specifically required both to repress natural killer cell-associated genes and to down-regulate a battery of stem cell or progenitor cell genes at the pivotal stage of commitment.